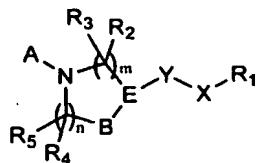


WE CLAIM

1. A compound of Formula I:



in which:

n is chosen from 0, 1 and 2; m is chosen from 1, 2 and 3;

R_1 is chosen from C_{6-10} aryl and C_{5-10} heteroaryl; wherein any aryl or heteroaryl of R_1 is optionally substituted by a radical chosen from C_{6-10} aryl C_{0-4} alkyl, C_{5-6} heteroaryl C_{0-4} alkyl, C_{3-8} cycloalkyl C_{0-4} alkyl, C_{3-8} heterocycloalkyl C_{0-4} alkyl or C_{1-10} alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by 1 to 5 radicals chosen from halo, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from $-S-$, $-S(O)-$, $-S(O)_2-$, $-NR_7-$ and $-O-$; wherein R_7 is chosen from hydrogen and C_{1-6} alkyl;

R_2 , R_3 , R_4 and R_5 are independently chosen from hydrogen, halo, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy;

A is chosen from $-X_1C(O)OR_7$, $-X_1OP(O)(OR_7)_2$, $-X_1P(O)(OR_7)_2$, $-X_1P(O)OR_7$, $-X_1S(O)_2OR_7$, $-X_1P(O)(R_7)OR_7$ and $1H$ -tetrazol-5-yl; wherein X_1 is chosen from a bond, C_{1-3} alkylene and C_{2-3} alkenylene and R_7 is chosen from hydrogen and C_{1-6} alkyl;

B is CR_8R_9 ; wherein R_8 and R_9 are independently chosen from hydrogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy;

E is chosen from CR_8 or N ; wherein R_8 is chosen from hydrogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy; or B is CR_9 and E is carbon and B and E are connected via a double bond;

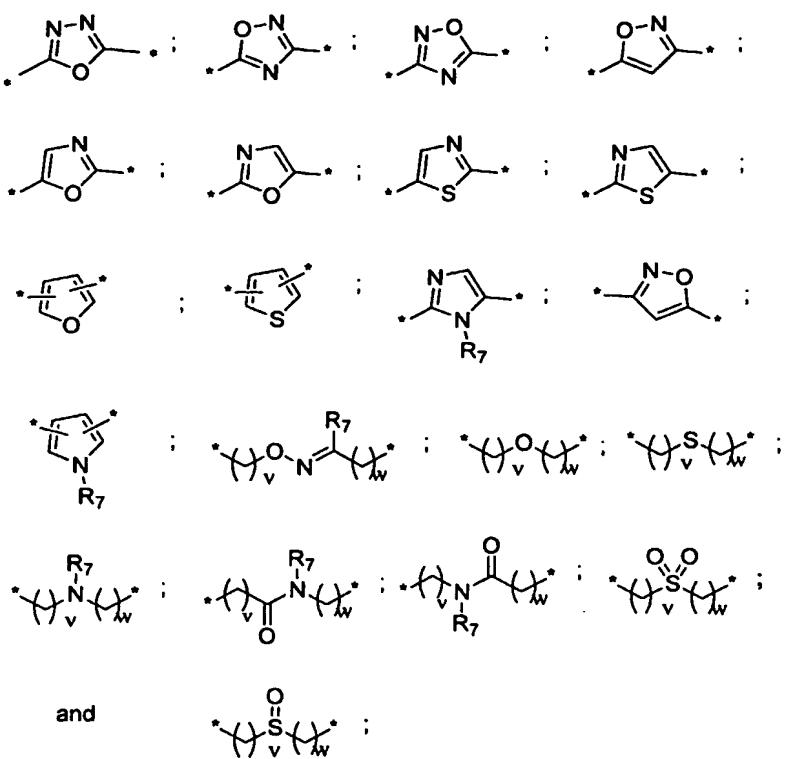
X is a bond or is chosen from $-X_1OX_2-$, $-X_1NR_7X_2-$, $-X_1C(O)NR_7X_2-$, $-X_1NR_7C(O)X_2-$, $-X_1S(O)X_2-$, $-X_1S(O)_2X_2-$, $-X_1SX_2-$, C₄₋₆heteroarylene and $-X_1ON=C(R_7)X_2-$; wherein X₁ and X₂ are independently chosen from a bond, C₁₋₃alkylene and C₂₋₃alkenylene; R₇ is chosen from hydrogen and C₁₋₆alkyl; and any heteroarylene of X is optionally substituted by a member of the group chosen from halo and C₁₋₆alkyl;

Y is chosen from C₆₋₁₀aryl and C₅₋₁₀heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydroxy, nitro, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted C₁₋₁₀alkyl and halo-substituted C₁₋₁₀alkoxy; and the pharmaceutically acceptable salts, hydrates, solvates, isomers and prodrugs thereof.

2. The compound of claim 1 in which R₁ is chosen from phenyl, naphthyl and thiophenyl optionally substituted by C₆₋₁₀arylC₀₋₄alkyl, C₅₋₆heteroarylC₀₋₄alkyl, C₃₋₈cycloalkylC₀₋₄alkyl, C₃₋₈heterocycloalkylC₀₋₄alkyl or C₁₋₁₀alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R₁ can be optionally substituted by 1 to 5 radicals chosen from halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy; and any alkyl group of R₁ can optionally have a methylene replaced by an atom or group chosen from $-S-$, $-S(O)-$, $-S(O)_2-$, $-NR_7-$ and $-O-$; wherein R₇ is hydrogen or C₁₋₆alkyl.

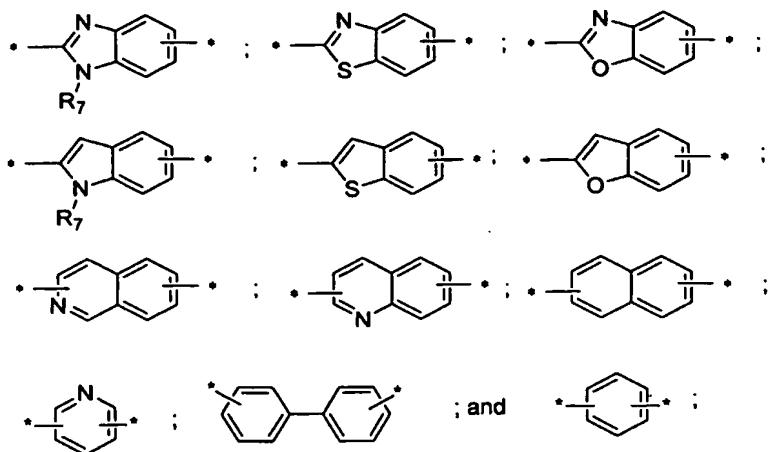
3. The compound of claim 1 in which A is chosen from $-X_1C(O)OR_7$ and 1*H*-tetrazol-5-yl; wherein X₁ is chosen from a bond, C₁₋₃alkylene and C₂₋₃alkenylene and R₇ is chosen from hydrogen and C₁₋₆alkyl.

4. The compound of claim 1 in which X is chosen from:



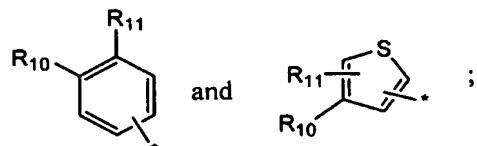
wherein the left and right asterisks of X indicate the point of attachment between R₁ and Y of Formula I, respectively; R₇ is chosen from hydrogen and C₁₋₆alkyl; v and w are independently 0, 1, 2 or 3.

5. The compound of claim 1 in which Y is chosen from:



wherein R₇ is hydrogen or C₁₋₆alkyl; and the left and right asterisks of Y indicate the point of attachment between X and E of Formula I, respectively.

6. The compound of claim 2 in which R₁ is chosen from:

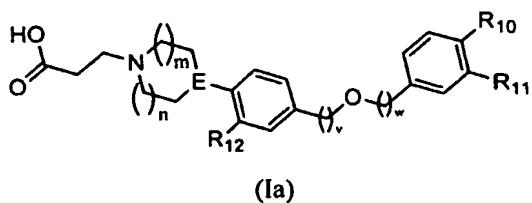


wherein the asterisk is the point of attachment of R₁ with X; R₁₀ is C₆₋₁₀arylC₀₋₄alkyl, C₅₋₆heteroarylC₀₋₄alkyl, C₃₋₈cycloalkylC₀₋₄alkyl, C₃₋₈heterocycloalkylC₀₋₄alkyl or C₁₋₁₀alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R₁₀ can be optionally substituted by 1 to 3 radicals chosen from halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy; and any alkyl group of R₁₀ can optionally have a methylene replaced by an atom or group chosen from -S-, -S(O)-, -S(O)₂-, -NR₇- and -O-; wherein R₇ is hydrogen or C₁₋₆alkyl; and R₁₁ is selected from halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy.

7. The compound of claim 2 selected from: 3-{4-[6-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyridin-3-yl]-piperazin-1-yl}-propionic acid; 3-{4-[6-(4-

Cyclohexyl-3-trifluoromethyl-phenoxy(methyl)-pyridin-3-yl}-piperazin-1-yl}-propionic acid; 3-{4-[6-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyridazin-3-yl]-piperazin-1-yl}-propionic acid; 3-{4-[2-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyrimidin-5-yl]-piperazin-1-yl}-propionic acid; 3-{4-Hydroxy-4-[2-(2-trifluoromethyl-biphenyl-4-yl)-benzo[b]thiophen-5-yl]-piperidin-1-yl}-propionic acid; 3-{4-[2-(2-Trifluoromethyl-biphenyl-4-yl)-benzo[b]thiophen-5-yl]-3,6-dihydro-2H-pyridin-1-yl}-propionic acid; 3-{3-{4-[3-(2-Trifluoromethyl-biphenyl-4-yl)-[1,2,4]oxadiazol-5-yl]-phenyl}-pyrrolidin-1-yl}-propionic acid; 3-(3-{3-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{3-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{4-[3-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(4-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-(3-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(4-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(4-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-(3-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-azetidin-1-yl)-propionic acid; 3-(3-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-azetidin-1-yl)-propionic acid; 3-(4-{4-[5-(3-Trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-{4-[6-(2-Trifluoromethyl-biphenyl-4-yloxy)methyl]-pyridin-3-yl}-piperazin-1-yl}-propionic acid; and 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-ylsulfanyl)methyl]-phenyl}-piperidin-1-yl}-propionic acid.

8. The compound of claim 2 of Formula Ia:



in which:

E is selected from N and CH;

m and n are independently selected from 0 and 1;

v and w are independently selected from 0 and 1;

R₁₀ is selected from cyclohexyl, piperidinyl, tetrahydro-thiopyran-4-yl, phenyl, phenoxy and phenylsulfanyl; wherein any cyclohexyl, piperidinyl, tetrahydro-thiopyran-4-yl, phenyl, phenoxy and phenylsulfanyl of R₁₀ can be optionally substituted by 1 to 3 radicals independently selected from methyl and isopropyl;

R₁₁ is selected from methyl, trifluoromethyl and ethyl; and

R₁₂ is selected from hydrogen, ethyl and methoxy.

9. The compound of claim 8 selected from: 3-{4-[4-(4-Cyclohexyl-3-methyl-phenoxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Piperidin-1-yl-3-trifluoromethyl-phenoxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-(4-{4-[3-Methyl-4-(tetrahydro-thiopyran-4-yl)-phenoxy)methyl]-phenyl}-piperidin-1-yl)-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-2-ethyl-phenyl]-piperazin-1-yl}-propionic acid; 3-{4-[4-(2-Methyl-biphenyl-4-yloxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{4-[4-(3'-Methyl-2-trifluoromethyl-biphenyl-4-yloxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxy)methyl]-phenyl}-pyrrolidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-ethyl-phenoxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-yloxy)methyl]-phenyl}-pyrrolidin-1-yl}-propionic acid; 3-{4-[4-(3,6-Dihydro-2H-thiopyran-4-yl)-3-trifluoromethyl-phenoxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-azetidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-yloxy)methyl]-phenyl]-azetidin-1-yl}-propionic acid; 3-{4-[2-Ethyl-4-(2-trifluoromethyl-biphenyl-4-yloxy)methyl]-phenyl}-piperidin-1-yl}-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-

benzyloxy)-2-ethyl-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4'-Methyl-2-trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Phenoxy-3-trifluoromethyl-phenoxy-methyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxy-methyl)-2-methoxy-phenyl]-piperazin-1-yl}-propionic acid; 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-azetidin-1-yl}-propionic acid; 3-{4-[4-(4-Isobutyl-3-trifluoromethyl-benzyloxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Phenylsulfanyl-3-trifluoromethyl-phenoxy-methyl)-phenyl]-piperidin-1-yl}-propionic acid; 1-(1H-Tetrazol-5-ylmethyl)-4-[4-(2-trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidine; 1-[2-(1H-Tetrazol-5-yl)-ethyl]-4-[4-(2-trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidine; 3-{4-[4-(2,4'-Dimethyl-biphenyl-4-yloxy-methyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2,4'-Dimethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Ethyl-biphenyl-4-yloxy-methyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Ethyl-3'-methyl-biphenyl-4-yloxy-methyl)-phenyl]-piperidin-1-yl}-propionic acid; (2-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxy-methyl)-phenyl]-piperidin-1-yl}-ethyl)-phosphonic acid; 2-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxy-methyl)-phenyl]-piperidin-1-yl}-ethanesulfonic acid; and Phosphoric acid mono-(2-{4-[4-(2-trifluoromethyl-biphenyl-4-yloxy-methyl)-phenyl]-piperidin-1-yl}-ethyl) ester.

10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a pharmaceutically acceptable excipient.

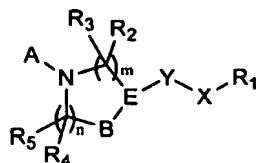
11. A method for treating a disease in an animal in which alteration of EDG/S1P receptor mediated signal transduction can prevent, inhibit or ameliorate the pathology and/or symptomology of the disease, which method comprises administering to the animal a therapeutically effective amount of a compound of Claim 1.

12. A method for preventing or treating disorders or diseases mediated by lymphocytes, for preventing or treating acute or chronic transplant rejection or T-cell

mediated inflammatory or autoimmune diseases, for inhibiting or controlling deregulated angiogenesis, or for preventing or treating diseases mediated by a neo-angiogenesis process or associated with deregulated angiogenesis in a subject comprising administering to the subject in need thereof an effective amount of a compound of claims I, or a pharmaceutically acceptable salt thereof.

13. The use of a compound of claim 1 in the manufacture of a medicament for treating a disease in an animal in which alteration of EDG/SIP receptor mediated signal transduction contributes to the pathology and/or symptomology of the disease.

14. A process for preparing a compound of Formula I:



in which:

n is chosen from 0, 1 and 2; m is chosen from 1, 2 and 3;

R₁ is chosen from C₆₋₁₀aryl and C₅₋₁₀heteroaryl; wherein any aryl or heteroaryl of R₁ is optionally substituted by a radical chosen from C₆₋₁₀arylC₀₋₄alkyl, C₅₋₆heteroarylC₀₋₄alkyl, C₃₋₈cycloalkylC₀₋₄alkyl, C₃₋₈heterocycloalkylC₀₋₄alkyl or C₁₋₁₀alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R₁ can be optionally substituted by 1 to 5 radicals chosen from halo, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy; and any alkyl group of R₁ can optionally have a methylene replaced by an atom or group chosen from -S-, -S(O)-, -S(O)₂-, -NR₇- and -O-; wherein R₇ is chosen from hydrogen and C₁₋₆alkyl;

R₂, R₃, R₄ and R₅ are independently chosen from hydrogen, halo, hydroxy, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy;

A is chosen from -X₁C(O)OR₇, -X₁OP(O)(OR₇)₂, -X₁P(O)(OR₇)₂, -X₁P(O)OR₇, -X₁S(O)₂OR₇, -X₁P(O)(R₇)OR₇ and 1*H*-tetrazol-5-yl; wherein X₁ is chosen from a bond, C₁₋₃alkylene and C₂₋₃alkenylene and R₇ is chosen from hydrogen and C₁₋₆alkyl;

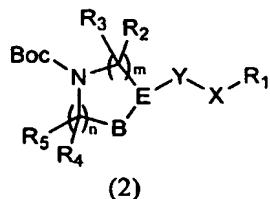
B is CR₈R₉; wherein R₈ and R₉ are independently chosen from hydrogen, hydroxy, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy;

E is chosen from CR₈ or N; wherein R₈ is chosen from hydrogen, hydroxy, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted-C₁₋₁₀alkyl and halo-substituted-C₁₋₁₀alkoxy; or B is CR₉ and E is carbon and B and E are connected via a double bond;

X is a bond or is chosen from -X₁OX₂₋, -X₁NR₇X₂₋, -X₁C(O)NR₇X₂₋, -X₁NR₇C(O)X₂₋, -X₁S(O)X₂₋, -X₁S(O)₂X₂₋, -X₁SX₂₋, C₄₋₆heteroarylene and -X₁ON=C(R₇)X₂₋; wherein X₁ and X₂ are independently chosen from a bond, C₁₋₃alkylene and C₂₋₃alkenylene; R₇ is chosen from hydrogen and C₁₋₆alkyl; and any heteroarylene of X is optionally substituted by a member of the group chosen from halo and C₁₋₆alkyl;

Y is chosen from C₆₋₁₀aryl and C₅₋₁₀heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydroxy, nitro, C₁₋₁₀alkyl, C₁₋₁₀alkoxy, halo-substituted C₁₋₁₀alkyl and halo-substituted C₁₋₁₀alkoxy; which process comprises:

(a) reacting a compound of formula 2:



with either *t*-butyl acrylate, acylonitrile/NaN₃ or bromoacetonitrile/NaN₃; wherein B, E, Y, X, R₁, R₂, R₃, R₄ and R₅ are as described above; and

(b) optionally converting a compound of the invention into a pharmaceutically acceptable salt;

(c) optionally converting a salt form of a compound of the invention to a non-salt form;

(d) optionally converting an unoxidized form of a compound of the invention into a pharmaceutically acceptable N-oxide;

(e) optionally converting an N-oxide form of a compound of the invention to its unoxidized form;

- (f) optionally resolving an individual isomer of a compound of the invention from a mixture of isomers;
- (g) optionally converting a non-derivatized compound of the invention into a pharmaceutically acceptable prodrug derivative; and
- (h) optionally converting a prodrug derivative of a compound of the invention to its non-derivatized form.